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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,469	09/24/2001	Stephen J. Benkovic	6460-18-1	1582

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EXAMINER	
FRONDA, CHRISTIAN L	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,469	BENKOVIC ET AL.	
	Examiner	Art Unit	
	Christian L Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-127 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-127 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Invention 1 Claim(s) 1-11, 14-40, 53-89, drawn to a non-naturally occurring nucleic acid molecule encoding a polypeptide comprising a first portion of a split intein, a second portion of a split intein, and a target peptide interposed between the first portion of a split intein and the second portion of a split intein; an expression vector comprising said nucleic acid; a host system comprising said nucleic acid; method for making a peptide molecule.

Invention 2 Claim(s) 12 and 13, drawn to a non-naturally occurring nucleic acid molecule encoding a polypeptide comprising a first portion of a split intein, a second portion of a split intein, a third portion of a split intein, and fourth portion of a split intein, wherein a first target peptide is interposed between the first portion of a split intein and the second portion of a split intein, and a second target peptide is interposed between the third portion of a split intein and the fourth portion of a split intein.

Invention 3 Claim(s) 41-52, drawn to a substantially pure polypeptide comprising a first portion of a split intein, a second portion of a split intein, and a target peptide interposed between the first portion of a split intein and the second portion of a split intein.

Invention 4 Claim(s) 90-92, drawn to a method for preparing a library of peptide molecules wherein the plurality of polypeptides are polypeptide that spontaneously splice in the host system to yield cyclized forms of the target peptides.

Invention 5 Claim(s) 90, 93, drawn to a method for preparing a library of peptide molecules wherein the plurality of nucleic acid molecules encoding a plurality of target peptides are produced by solid phase synthesis.

Invention 6 Claim(s) 90, 94, drawn to a method for preparing a library of peptide molecules wherein the plurality of nucleic acid molecules encoding a plurality of target peptides are produced using polymerase chain reaction.

Invention 7 Claim(s) 90, 95, 96, drawn to a method for preparing a library of peptide molecules wherein the plurality of nucleic acid molecules encoding a plurality of target peptides are produced by enzymatically digesting a larger nucleic acid molecule.

Invention 8 Claim(s) 98-103, drawn to a method of screening a peptide molecule for ability to specifically bind a target molecule by observing fluorescent signal.

Invention 9 Claim(s) 98, 101, 104, drawn to a method of screening a peptide molecule for ability to specifically bind a target molecule by analyzing the cell cycle of an organism.

Invention 10 Claim(s) 98, 101, 105, drawn to a method of screening a peptide molecule for ability to specifically bind a target molecule by analyzing the reproduction of an organism.

Invention 11 Claim(s) 98, 101, 106, 107, drawn to a method of screening a peptide molecule for ability to specifically bind a membrane associated molecule.

Invention 12 Claim(s) 98, 101, 106, 108, 109, drawn to a method of screening a peptide molecule for ability to specifically bind a nuclear molecule.

Invention 13 Claim(s) 98, 101, 106, 108, 110, 111, drawn to a method of screening a peptide molecule for ability to specifically bind an organelle.

Invention 14 Claim(s) 98, 101, 112 , drawn to a method of screening a peptide molecule for ability to specifically bind an extracellular molecule.

Invention 15 Claim(s) 98, 113-115, drawn to a method of screening a peptide molecule for ability to modulate a biochemical reaction by observing a fluorescent signal.

Invention 16 Claim(s) 98, 113, 116, drawn to a method of screening a peptide molecule for ability to modulate a biochemical reaction by analyzing the cell cycle of an organism.

Invention 17 Claim(s) 98, 113, 117, drawn to a method of screening a peptide molecule for ability to modulate a biochemical reaction by analyzing the reproduction of an organism.

Invention 18 Claim(s) 98, 113, 118, 119, drawn to a method of screening a peptide molecule for ability to modulate an intracellular metabolic event.

Invention 19 Claim(s) 98, 113, 118, 120, drawn to a method of screening a peptide molecule for ability to modulate a membrane-associated event.

Invention 20 Claim(s) 98, 113, 118, 121, drawn to a method of screening a peptide molecule for ability to modulate a nuclear event.

Invention 21 Claim(s) 98, 113, 122, drawn to a method of screening a peptide molecule for ability to modulate an extracellular reaction.

Invention 22 Claim(s) 125, drawn to a method for purifying a cyclic peptide from a mixture comprising adding to the support a reagent that makes a cyclic peptide from the splicing intermediate and eluting the cyclic peptide from the support.

Invention 23 Claim(s) 126, drawn to a method for purifying a cyclic peptide from a mixture comprising eluting the splicing intermediate from the support and adding a reagent to the eluted splicing intermediate that makes a cyclic peptide from the splicing intermediate .

Invention 24 Claim(s) 127, drawn to a method for purifying a target molecule that binds a splicing intermediate.

2. The inventions listed as Inventions 1-24 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

A same or corresponding technical feature shared among Inventions 1 and 3-24 is a polypeptide comprising a first portion of a split intein, a second portion of a split intein, and a target peptide interposed between the first portion of a split intein and the second portion of a split intein. However, this technical feature has already been taught by Holford et al. (Structure. 1998 Aug 15;6(8):951-6.) [this reference is cited in the PCT International Search Report of

PCT/US99/30162 and is not attached to the instant Office Action].

Holford et al. teach the concept of how head-to-tail cyclized recombinant peptides and proteins could be made using the taught Expressed Protein Ligation (EPL), where introduction of an N-terminal cysteine and a C-terminal thioester within the same polypeptide chain allows for intramolecular native chemical ligation; and that this process has been used to prepare synthetic circular protein domain (see entire document, especially p. 955, penultimate paragraph)

The specification defines the word "intein" is a polypeptide sequence that can catalyze a splicing reaction during post-translational processing of a protein (see p. 13, lines 3-5). Thus, when the teachings Holford et al. are read in view of this definition of "intein", the N-terminal polypeptide sequence of the recombinant protein containing the introduced N-terminal cycteine is deemed to be the first portion of a split intein; the C-terminal polypeptide sequence containing the introduced C-terminal thioester is deemed to be the second portion of a split intein; and the polypeptide sequence in between is deemed to be the target peptide that is to be cyclized.

Thus, the technical feature is not special since it was known in the prior art and therefore cannot make a contribution over the prior art.

Invention 3 and Inventions (1, 3-24) do not share a same or corresponding technical feature. The technical feature of Invention 3 is a polypeptide comprising a first portion of a split intein, a second portion of a split intein, a third portion of a split intein, and fourth portion of a split intein, wherein a first target peptide is interposed between the first portion of a split intein and the second portion of a split intein, and a second target peptide is interposed between the third portion of a split intein and the fourth portion of a split intein. The technical feature of Invention 3 is structurally different and not homologous to the technical feature of Inventions (1, 3-24).

3. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The

examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

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